REMARKS

Reconsideration of the subject application in view of the following remarks is respectfully requested.

Claims 50-95 are currently pending in this application. By this amendment, Claim 96 has been cancelled and Claims 50, 70, 73 and 92 have been amended to point out with particularity what was believed to be already inherently claimed and anticipate potential antecedent basis issues. No new matter has been added to the subject application by this amendment, nor have any new issues been raised.

The Office Action

In the outstanding Office Action, Claims 50-96 were rejected under 35 U.S.C. §102(a) as being allegedly anticipated by WO 98/07414. Claims 50-96 also stand rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over U.S. Pat. No. 5,827,541 to Yarwood by itself or in further combination with U.S. Pat. No. 5,976,577 to Green or U.S. Pat. No. 5,346,702 to Na et al.

The Examiner noted in the Office Action that references cited on a PTO-1449 form have not been considered because their relevance has not been stated and copies have not been provided. Applicants believe that copies for all non-U.S. Patent references cited on any PTO-1449 form submitted in regard to the instant application have now been submitted, and confirmation of the same is respectfully requested.

Response by Applicant

Applicants traverse the Examiner's rejections primarily because of the reasons set forth herein below. Applicants believe the claims as examined were directed to subject matter which was neither disclosed nor suggested by the cited references in the office action. By this amendment, Applicants have amended the claims of the instant application in an effort to anticipate antecedent basis issues and advance prosecution, but not in acquiescence of any rejection thereto. Applicants respectfully submit that the claims as now presented are also directed to subject matter which is neither disclosed nor suggested by the cited references by themselves or in combination with any other references cited in the office action. Furthermore, Applicants believe these claims are now in condition for allowance. For illustrative purposes, Applicants have addressed the rejections in the outstanding office action as if the rejections had been asserted against the claims in their newly amended form.

Claim Rejection – 35 U.S.C. § 102

Applicants contend that this rejection should be withdrawn primarily because the instant application as presently claimed is not anticipated by the cited reference.

With regard to anticipation, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed.Cir. 1987). The identical invention must be shown in as complete detail as is contained in the... claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim.

WO 98/07414 is directed to "preparing submicron size particles using a combination of surface modifier(s) with a phospholipid," among other things. (See WO 98/07414, pg. 2, ln. 26-27). The "phospholipid and surface modifier(s) are adsorbed on to the surfaces of drug particles in sufficient quantity to retard drug particle growth, reduce drug average particle size from 5 to 100 μm to submicron and micron size particles by one or combination of methods known in the art, such as sonication, homogenization, milling, microfluidization, precipitation or recrystallization or precipation from a supercritical fluid and maintain submicron and micron size particles on subsequent storage as suspension or solid dosage form." (See WO 98/07414, pg. 4, ln. 1-8). The formulations of WO 98/07414 may be "lyophilized into powders, which can be resuspended or filled into capsules or converted into granules or tablets." (See WO 98/07414, pg. 4, ln. 14-17).

In contrast, Applicants' invention as claimed is directed to a process involving steps not disclosed in this reference. For example, the instant independent claims include steps relating to the admixing of a suspension containing drug particles with a matrix-forming bulking/releasing agent, or agents, among other things, to produce a solid having surface stabilized drug particles in a matrix which are released upon contact with an aqueous environment. Clearly, steps such as these which are included in independent Claims 50 and 73 are not disclosed in this reference.

Thus, it is respectfully submitted that independent Claims 50 and 73 are not anticipated by WO 98/07414, and the 102 rejection should be withdrawn. Since the claims that depend from Claims 50 and 73, namely Claims 51-72 and 74-92, provide further limitations thereto, it is respectfully submitted that the dependent claims are also not rendered anticipated by the cited reference.

Claim Rejections – 35 U.S.C. § 103

Applicants contend that the Examiner has not satisfied the burden necessary for establishing a *prima facie* case of obviousness, as alleged in the outstanding office action.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant"s disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

103 Rejection based on Yarwood by itself

Clearly, U.S. Pat. No. 5,827,541 to Yarwood (hereinafter referred to as "Yarwood") is directed to a similar idea. However, Applicants respectfully disagree with the Examiner's contention that Yarwood provides sufficient support for establishing *prima facie* obviousness of the presently claimed invention. Applicants' process as now claimed is neither disclosed nor anticipated by Yarwood alone, or combined with any other reference.

First, Applicants contend that the mere mention of the possibility that another surfactant than that specifically named in Yarwood would render obvious the limitation relating to surface stabilizing agents and phospholipids in Applicant's invention as now claimed.

Although Yarwood states that any "surfactant which fulfils the requirement of pharmaceutical acceptability may be used in the invention," the Examiner admits that Yarwood

does not disclose phospholipids as the surfactants, nor does it teach a combination of surfactants. (See Page 3 of the outstanding Office Action).

Even if this statement in Yarwood could be found to suggest using another surfactant in the method disclosed which "fulfils the requirement of pharmaceutical acceptability," it would still be technically deficient to render Applicants' method obvious, as now claimed.

Yarwood provides no guidance for selecting any other surfactant, other than it should be pharmaceutically acceptable, as stated above. Thus, one skilled in the art presumably motivated by Yarwood to employ another surfactant, would be forced to conduct an expensive and time-consuming iterative process to develop a method which enables surface stabilized drug particles to form "a suspension without irreversible particle aggregation and/or particle agglomeration and without particle size growth" upon contact with an aqueous environment," among other things, as now claimed. Applicants point out that it has been held that not only must there be some reasonable expectation of success in the references themselves to support a §103 rejection, but the prior art or surrounding circumstances must render the Applicants' claimed invention obvious to do rather than obvious to try. *In re Tomlinson,* 150 USPQ 623 (CCPA 1966).

In other words, Applicants contend that one skilled in the art would not be motivated by a sole statement in Yarwood to modify its teachings to develop a method as presently claimed by Applicants, absent some other teaching suggesting Applicants' process as claimed. The Courts further support this contention by holding that the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). It has also been established that even if all elements of a claim are disclosed in various prior art references, the claimed invention taken as a whole cannot be said to be obvious without some

reason given in the prior art why one of ordinary skill would have been prompted to combine the teachings of the references to arrive at the claimed invention. *In re Regel,* 188 USPQ 132 (CCPA 1975).

These holdings are particularly on point in this instance, primarily because the sole statement in Yarwood which is directed to surfactants fails to provide the requisite desirability, reason or motivation that one skilled in the art would need to modify the Yarwood process so that it included "one or more surface stabilizing agents, one of which is a phospholipid" in a method such as that now claimed by Applicants in Claims 50 and 73. Thus, this rejection is improper and should be withdrawn.

103 Rejection based on Yarwood and Na

Combining Yarwood with U.S. Pat. No. 5,346,702 to Na et al. (hereinafter referred to as "Na") does not cure the deficiencies relating to the 103 rejection based on Yarwood by itself. Na discloses a composition comprised of nanoparticles containing an X-ray diagnostic compound having a surface modifier adsorbed on the surface thereof and a non-ionic cloud point modifier associated therewith, which cloud point modifier is present in an amount sufficient to increase the cloud point of the surface modifier. (See Na, col. 2, lin. 36-41). The composition comprises particles in an amount sufficient to maintain an effective average particle size of less than 400 nm. (See Na, col. 3, lin. 35-40).

Using the standards set forth above, Na does not provide one skilled in the art with the requisite motivation to combine its teachings with that of Yarwood in a way that would anticipate Applicants invention as now claimed.

For instance, Na is not in the same field as Yarwood, nor is it in the same field as Applicants' invention as now claimed. It is non-analogous art, and in such instances, Courts have held that in order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned." *In re Oetiker*, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). This rejection is improper for at least this reason.

Further, Na is directed to a composition having an average particle size of less than 400 nm, which is below the range claimed by Applicants, that is, Applicants' claims are directed to a mean volume weighted particle size of the water-insoluble or poorly water-soluble drug in the suspension that ranges between about 0.05 and about 10 micrometers. In this regard, the Courts have held that if a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). Courts have further held that if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959)

Applicants contend that in accordance with these holdings, the teachings of Na, which is directed to non-analogous subject matter involving particles outside of the particle range of Applicants' invention as now claimed, can not properly be combined with Yarwood to formulate an obviousness rejection, because it would render both Yarwood and Na unsatisfactory for their respective intended purposes and the resulting modification would differ in its principle of

operation from either Yarwood or Na. The rejection should be withdrawn for at least this reason.

Thus, Applicants submit that this rejection is improper and should be withdrawn.

103 Rejection based on Yarwood and Green

U.S. Pat. No. 5,976,577 to Green (hereinafter referred to as "Green") also fails to cure the deficiencies of Yarwood. Green discloses a method for producing a fast dispersing freeze-dried dosage form containing drug particles which may be uncoated or coated with a polymer or lipid material which exhibit minimal release of the drug in the mouth." (See Green, col 2, lin. 44-48). Green further discloses that its method is "achieved by using coarse coated drug particles," among other things. Green teaches that these coarse particles "may have a size of up to 1 millimeter, although the average size is generally up to about 500 μm, for example 75 to 400 μm, more usually in the region of about 100-300 μm," and further that "in this size range, it is possible to apply a uniform intact coating on the particle in order to achieve efficient freeze-dried dosage forms with slow drug release rate." (See Green, col. 3, lin. 15-21).

Like Na, Green is arguably not in the same field as Yarwood, or Applicants' invention as now claimed since Green is not reasonably pertinent to the particular problem with which the inventor was concerned." *In re Oetiker, infra.* Green is concerned with delaying the release of the drug "for a time at least sufficient to mask the taste in the mouth before swallowing, and typically for a longer period of time to provide controlled or sustained release of the drug after swallowing." (See Green, col. 2, lin. 54-57). In contrast, Applicants' claimed invention is directed to decreasing agglomeration and increasing bioavailability.

Green also teaches that the coarse particles can be coated or uncoated, whereas Applicant's invention is directed to surface modified particles, and importantly, teaches that coarse particles, which are much larger than the particle size limitations of Applicants' claims, are vital to obtaining the benefit of Green's teachings. As shown above, Applicants' claims are directed to a mean volume weighted particle size of the water-insoluble or poorly water-soluble drug in the suspension that ranges between about 0.05 and about 10 micrometers.

Clearly, a combination of Green and Yarwood would render both Yarwood and Green unsatisfactory for their respective intended purposes, and the modification proposed would result in a change in the principle of operation of both. As provided by the Courts and discussed above, in such situations there can be no suggestion or motivation to make the proposed modification, and the teachings of the Yarwood and Green, just like Yarwood and Na, are not sufficient to render the claims *prima facie* obvious. The rejection should be withdrawn for at least this reason.

Conclusion

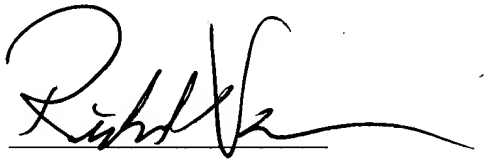
Since independent claims 50 and 73 contain limitations which are neither taught nor suggested by the cited references, either alone or combined, these claims are neither rendered anticipated nor obvious. Furthermore, since the claims that depend from these independent claims provide further limitations thereto, the dependent claims, namely claims 51-72 and 74-95, are also not rendered anticipated or obvious by the cited references, either alone or combined.

Accordingly, withdrawal of the rejections are therefore respectfully requested. It is respectfully submitted that as a result of this amendment and discussion relating thereto, all of the claims presently pending in this application, namely Claims 1-37 and 60-84 are in condition for allowance, and such action is earnestly solicited.

Applicants submit this response without prejudice to any of Applicants' rights, such as the right to proffer additional arguments and/or evidence in support of arguments contained herein or newly developed arguments, against these rejections or others, in the present application or any application which claims priority of the present application.

If the Examiner believes that a personal or telephonic interview may facilitate resolution of any remaining matters, Applicants' representative may be contacted at the number indicated below.

Respectfully submitted,



Richard H. Newman, Reg. No. 41,222
Edwards & Angell, LLP
Three Stamford Plaza
301 Tresser Blvd., 6th Floor
Stamford, CT 06901
Tel. No. (203) 353-6836

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